December 19, 2022

Tonix Pharmaceuticals Achieves Enrollment of First 50 Percent of Participants in the RESILIENT Study, a Potentially Pivotal Confirmatory Phase 3 Study of TNX-102 SL for the Management of Fibromyalgia

Results from Planned Interim Analysis of First 50 Percent of Participants Expected Second Quarter 2023

Topline Results Expected Fourth Quarter 2023

Positive Outcome in RESILIENT, Together with Results from Previous Positive Phase 3 RELIEF Study, Would Support Submission of an NDA

CHATHAM, N.J., Dec. 19, 2022 (GLOBE NEWSWIRE) -- Tonix Pharmaceuticals Holding Corp. (Nasdaq: TNXP) (Tonix or the Company), a clinical-stage biopharmaceutical company, today announced that the first 50% of participants have been randomized in the Phase 3 RESILIENT study of TNX-102 SL (cyclobenzaprine HCl sublingual tablets) 5.6 mg for the management of fibromyalgia. An interim analysis by an Independent Data Monitoring Committee (IDMC) of the first 50% of randomized participants for a potential sample size adjustment or early stop for futility is expected in the second quarter of 2023.

TNX-102 SL is in mid-Phase 3 development for the management of fibromyalgia, a chronic pain disorder that afflicts between 6 and 12 million adults in the U.S., of which 90 percent are women. Despite dissatisfaction with currently marketed products, no new treatment for fibromyalgia has been approved by the FDA since 2009.

In December 2020, Tonix reported positive results from the first Phase 3 study (RELIEF) of TNX-102 SL 5.6 mg for the management of fibromyalgia (primary endpoint, $p=0.010$). Several secondary measures in RELIEF highlighted the broad effects of TNX-102 SL across several cardinal symptoms of fibromyalgia beyond pain. In March 2022, Tonix reported results of a subsequent Phase 3 study (RALLY) in which TNX-102 SL did not achieve statistical significance on the primary endpoint ($p=0.115$). Relative to the previous positive Phase 3 study (RELIEF), RALLY had an unexpected increase in study participant adverse event-related discontinuations in both the drug and placebo groups. TNX-102 SL was generally well tolerated in both studies with an adverse event profile comparable to prior studies, and no new safety signals observed.

“We are pleased to have reached this important milestone in our ongoing development of TNX-102 SL for fibromyalgia. RESILIENT is a potentially pivotal and confirmatory Phase 3 study, and we look forward to the IDMC's assessment of interim results in the second quarter of 2023,” said Seth Lederman, M.D., Chief Executive Officer of Tonix Pharmaceuticals. “Fibromyalgia is a complex syndrome in which many patients remain unsatisfied by existing treatment options. Approximately one-fourth of people with fibromyalgia resort to prescription opioids for analgesia[1]. TNX-102 SL is a centrally acting analgesic that has the potential to be a new non-addictive, non-opioid bedtime medication for the management of fibromyalgia with broad spectrum symptom coverage.”

[1]Sarmento, CVM, et al. (2019) “Opioid prescription patterns among patients with fibromyalgia.” J Opioid Manag. 15(6):469-477. doi: 10.5055/jom.2019.0537. PMID: 31850508

About the Phase 3 RESILIENT Study

The RESILIENT study is a double-blind, randomized, placebo-controlled trial designed to evaluate the efficacy and safety of TNX-102 SL (cyclobenzaprine HCl sublingual tablets) in the management of fibromyalgia. The two-arm trial is expected to enroll approximately 470 participants in the U.S. The first two weeks of treatment consist of a run-in period in which participants start on TNX-102 SL 2.8 mg (1 tablet) or placebo. Thereafter, all participants increase their dose to TNX-102 SL 5.6 mg (2 x 2.8 mg tablets) or two placebo tablets for the remaining 12 weeks. The primary endpoint is the daily diary pain severity score change (TNX-102 SL 5.6 mg vs. placebo) from baseline to Week 14 (using the weekly averages of the daily numerical rating scale scores), analyzed by mixed model repeated measures with multiple imputation. An interim analysis by an Independent Data Monitoring Committee will be conducted on the primary endpoint based on the first 50% of enrolled participants for a potential sample size adjustment or early stop for futility.

For more information, see ClinicalTrials.gov Identifier: NCT05273749.

About Fibromyalgia

Fibromyalgia is a chronic pain disorder that is understood to result from amplified sensory and pain signaling within the central nervous system. Fibromyalgia afflicts an estimated 6-12 million adults in the U.S., approximately 90% of whom are women. Symptoms of fibromyalgia include chronic widespread pain, nonrestorative sleep, fatigue, and morning stiffness. Other associated symptoms include cognitive dysfunction and mood disturbances, including anxiety and depression. Individuals suffering from fibromyalgia struggle with their daily activities, have impaired quality of life, and frequently are disabled. Physicians and patients report common dissatisfaction with currently marketed products.

About TNX-102 SL

TNX-102 SL is a patented sublingual tablet formulation of cyclobenzaprine hydrochloride which provides rapid transmucosal absorption and reduced production of a long half-life active metabolite, norcyclobenzaprine, due to bypass of first-pass hepatic metabolism. As a multifunctional agent with potent binding and antagonist activities at the 5-HT2A-serotonergic, α1-adrenergic, H1-histaminergic, and M1-muscarinic receptors, TNX-102 SL is in development as a daily bedtime treatment for fibromyalgia, PTSD, Long COVID (formally

known as post-acute sequelae of COVID-19 [PASC]), alcohol use disorder and agitation in Alzheimer's disease. The United States Patent and Trademark Office (USPTO) issued United States Patent No. 9636408 in May 2017, Patent No. 9956188 in May 2018, Patent No. 10117936 in November 2018, Patent No. 10,357,465 in July 2019, and Patent No. 10736859 in August 2020. The Protectic™ protective eutectic and Angstro-Technology™ formulation claimed in the patent are important elements of Tonix's proprietary TNX-102 SL composition. These patents are expected to provide TNX-102 SL, upon NDA approval, with U.S. market exclusivity until 2034/2035.

Tonix Pharmaceuticals Holding Corp.*

Tonix is a clinical-stage biopharmaceutical company focused on discovering, licensing, acquiring and developing therapeutics to treat and prevent human disease and alleviate suffering. Tonix's portfolio is composed of central nervous system (CNS), rare disease, immunology and infectious disease product candidates. Tonix's CNS portfolio includes both small molecules and biologics to treat pain, neurologic, psychiatric and addiction conditions. Tonix's lead CNS candidate, TNX-102 SL (cyclobenzaprine HCl sublingual tablet), is in mid-Phase 3 development for the management of fibromyalgia with a new Phase 3 study launched in the second quarter of 2022 and interim data expected in the second quarter of 2023. TNX-102 SL is also being developed to treat Long COVID, a chronic post-acute COVID-19 condition. Tonix initiated a Phase 2 study in Long COVID in the third quarter of 2022 and expects interim data in the third quarter of 2023. TNX-1300 (cocaine esterase) is a biologic designed to treat cocaine intoxication and has been granted Breakthrough Therapy designation by the FDA. A Phase 2 study of TNX-1300 is expected to be initiated in the first quarter of 2023. TNX-1900 (intranasal potentiated oxytocin), a small molecule in development for chronic migraine, is expected to enter the clinic with a Phase 2 study in the first quarter of 2023. TNX-601 ER (tianeptine hemioxalate extended-release tablets) is a once-daily formulation of tianeptine being developed as a potential treatment for major depressive disorder (MDD) with a Phase 2 study expected to be initiated in the first quarter of 2023. Tonix's rare disease portfolio includes TNX-2900 (intranasal potentiated oxytocin) for the treatment of Prader-Willi syndrome. TNX-2900 has been granted Orphan Drug designation by the FDA. Tonix's immunology portfolio includes biologics to address organ transplant rejection, autoimmunity and cancer, including TNX-1500, which is a humanized monoclonal antibody targeting CD40-ligand (CD40L or CD154) being developed for the prevention of allograft and xenograft rejection and for the treatment of autoimmune diseases. A Phase 1 study of TNX-1500 is expected to be initiated in the first half of 2023. Tonix's infectious disease pipeline consists of a vaccine in development to prevent smallpox and monkeypox, next-generation vaccines to prevent COVID-19, and a platform to make fully human monoclonal antibodies to treat COVID-19. TNX-801, Tonix's vaccine in development to prevent smallpox and monkeypox, also serves as the live virus vaccine platform or recombinant pox vaccine (RPV) platform for other infectious diseases. A Phase 1 study of TNX-801 is expected to be initiated in Kenya in the second half of 2023. Tonix's lead vaccine candidate for COVID-19 is TNX-1850, a live virus vaccines based on Tonix's recombinant pox live virus vector vaccine platform.

**All of Tonix's product candidates are investigational new drugs or biologics and have not been approved for any indication.*

This press release and further information about Tonix can be found at

www.tonixpharma.com.

Forward Looking Statements

Certain statements in this press release are forward-looking within the meaning of the Private Securities Litigation Reform Act of 1995. These statements may be identified by the use of forward-looking words such as “anticipate,” “believe,” “forecast,” “estimate,” “expect,” and “intend,” among others. These forward-looking statements are based on Tonix's current expectations and actual results could differ materially. There are a number of factors that could cause actual events to differ materially from those indicated by such forward-looking statements. These factors include, but are not limited to, risks related to the failure to obtain FDA clearances or approvals and noncompliance with FDA regulations; delays and uncertainties caused by the global COVID-19 pandemic; risks related to the timing and progress of clinical development of our product candidates; our need for additional financing; uncertainties of patent protection and litigation; uncertainties of government or third party payor reimbursement; limited research and development efforts and dependence upon third parties; and substantial competition. As with any pharmaceutical under development, there are significant risks in the development, regulatory approval and commercialization of new products. Tonix does not undertake an obligation to update or revise any forward-looking statement. Investors should read the risk factors set forth in the Annual Report on Form 10-K for the year ended December 31, 2021, as filed with the Securities and Exchange Commission (the “SEC”) on March 14, 2022, and periodic reports filed with the SEC on or after the date thereof. All of Tonix's forward-looking statements are expressly qualified by all such risk factors and other cautionary statements. The information set forth herein speaks only as of the date thereof.

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